Listing of Claims of the Application

1.(Original) A method for detecting a chronic dementia disease or a predisposition to a chronic dementia disease in a patient in need thereof, comprising the steps of

obtaining a biological sample from said patient,

determining a concentration of at least one VGF protein or VGFARP peptide in the biological sample, and

comparing the concentration of the at least one VGF protein or VGFARP peptide in the biological sample to the concentration of the same protein or peptide in a control sample, wherein a difference between the concentration of the VGF protein or VGFARP peptide in the biological sample compared to the concentration of the VGF protein or VGFARP peptide in the control sample is indicative of chronic dementia disease or a predisposition to a chronic dementia disease.

2. (Original) The method of claim 1, wherein the at least one VGF protein or VGFARP peptide is selected from the group consisting of: SEQ ID NO:43; SEQ ID NO:44;a mutant of SEQ ID NO:43 in which the amino acid sequence of the mutant differs by a maximum of 20% from the amino acid sequence of SEQ ID NO:43; a mutant of SEQ ID NO:44 in which the amino acid sequence of the mutant differs by a maximum of 20% from the amino acid sequence of SEQ ID NO:44; a protein that represents a naturally occurring allele of a VGF protein; a peptide derivate derived from a naturally occurring allele of a VGF protein; a peptide derivate derived from a VGFARP peptide; a VGFARP peptide mutant that differs by a maximum of 2 amino acids from the corresponding unmutated VGFARP peptide.

3. (Original) The method of claim 2, wherein said VGFARP peptide is selected from the group consisting of: SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ

ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:41, and SEQ ID NO:42.

4. (Original) The method of claim 2 wherein the at least one VGF protein or VGFARP peptide is chemically modified.

5. (Original) The method of claim 2 wherein the at least one VGF protein or VGFARP peptide is post-translationally modified.

6. (Original) The method of claim 1 wherein said method is carried out in combination with other diagnostic methods for chronic dementia diseases to increase the sensitivity and/or specificity thereof.

7. (Original) The method of claim 1 wherein the dementia disease is selected from the group consisting of Alzheimer's disease or a related neurological disease; Lewy body dementia; and vascular dementia.

8. (Original) The method of claim 1 wherein for a positive detection of the disease the concentration of the at least one VGF protein or VGFARP peptide is raised or lowered relative to the concentration of the VGF protein or VGFARP peptide in a control sample.

9. (Original) The method of claim 1 wherein the method is used to determine a parameter selected from the group consisting of: the severity of the disease, prognosis of the course of the disease, diagnosis of preliminary stages of neurological diseases, and mild cognitive impairment (MCI).

10. (Original) The method of claim 1 wherein the biological sample is selected from the group consisting of cerebrospinal fluid, serum, plasma, urine, synovial fluid, stool, tear fluid, sputum and a tissue homogenate

11. (Original) The method of claim 1 wherein the at least one VGF protein or VGFARP peptide is identified by mass spectrometry.

12. (Original) The method of claim 11, wherein identification of the at least one VGF protein or VGFARP peptide by mass spectroscopy includes the determination of at least one of the theoretical monoisotopic mass peaks selected from the group consisting of 3666.8278 / 3950.9875 / 3567.7594 / 3595.7907 / 3879.9504 / 3401.6852 / 3614.8077 / 3685.8448 / 3302.6167 / 3173.5741 / 3955.9889 / 1336.6735 / 2503.1827 / ≥727.3501 /≥ 851.4137 / ≥ 730.3246 / 3745.7343 / 1235.5782 / [3] 833.4395 / 7518.2744 / 2031.8981 / 2418.0419 / 4806.0408 / 3456.5513 / 4806.0408 / 4058.7043 / 5776.6294 / 6618.0363 / 1380.7249 / ≥946.4468 /≥ 862.3192 /≥ 961.4063 / 3903.0180 / 3787.9911 /≥ 920.4828 / 656.3242 / 3782.8976 / 1886.8970 / 1672.7653 / ≥ 792.3501 / 3343.4672 and 2220.1889 dalton.

13. (Original) The method of claim 1, wherein the at least one VGF protein or VGFARP peptide is identified with an immunological test.

14. (Original) The method of claim 13, wherein said immunological test is selected from the group consisting of enzyme linked immuno sorbent assay (ELISA), a radioimmunoassay, and a Western blot.

15. (Original) The method of claim 13, wherein the at least one VGF protein or VGFARP peptide is identified using a substance that binds to the protein or peptide.

16. (Original) The method of claim 15, wherein the substance that binds to the at least one VGF protein or VGFARP peptide is selected from the group consisting of an antibody, an antibody fragment, a phage particle, and an affinity matrix.

17. (Original) The method of claim 1 further comprising the step of chromatographically fractionating said biological sample prior to said determining step.

18. (Original) The method of claim 17 wherein said step of chromatographically fractionating said biological sample is carried out using reverse phase chromatography or high resolution reverse phase chromatography.

19. (Original) The method of claim 1 further comprising the step of fractionating the biological sample by precipitation reactions or liquid phase separations prior to said determining step.

20. (Original) The method of claim 1 wherein said step of determining is carried out using antibodies against at least one VGF protein or VGFARP peptide.

21. (Original) The method of claim 1 wherein said step of determining is carried out by detection of nucleic acids encoding at least one VGF protein or VGFARP peptide.

22. (Original) The method of claim 21 wherein the detection of nucleic acids is carried out using Northern blots, reverse transcriptase PCR or quantitative PCR.

23. (Original) A method for diagnosing a neurological disease in a patient, comprising the step of

obtaining a biological sample from said patient,

determining a concentration of at least one VGF protein or VGFARP peptide in the biological sample, and

comparing the concentration of the at least one VGF protein or VGFARP peptide in the

biological sample to the concentration of the same protein or peptide in a control sample, wherein a difference between the concentration of the VGF protein or VGFARP peptide in the biological sample compared to the concentration of the VGF protein or VGFARP peptide in the control sample is indicative of a neurological disease.

24. (Original) The method of claim 23 wherein said step of determining is carried out using antibodies against at least one VGF protein or VGFARP peptide.

25. (Original) The method of claim 23 wherein said step of determining is carried out by detection of nucleic acids encoding at least one VGF protein or VGFARP peptide.

26. (Original) The method of claim 25 wherein the detection of nucleic acids is carried out by using Northern blots, reverse transcriptase PCR or quantitative PCR.

27. (Original) The method of claim 23, wherein the method is used to monitor the efficacy of a therapy for a neurological disease.

28. (Original) The method of claim 23, wherein the method is used for stratifying patients who are suitable for therapies or clinical studies of neurological diseases.

29. (Original) The method of claim 23, wherein the neurological disease is selected from the group consisting of chronic dementia disease and Alzheimer's disease.

30. (Original) A method for prophylaxis or treatment of a neurological disease in a patient in need thereof, comprising the step of

administering to the patient a substance that causes modulation of the concentration of at least one VGF protein or VGFARP peptide in a quantity sufficient to prevent or treat the neurological disease.

31. (Original) The method of claim 30, wherein the neurological disease is selected from the group consisting of chronic dementia disease and Alzheimer's disease.

32. (Original) The method of claim 30, wherein the modulation is a reduction in concentration of the at least one VGF protein or VGFARP peptide.

33. (Original) A method of claim 30, wherein the modulation is an increase in concentration of the at least one VGF protein or VGFARP peptide.

34.(Original) The method of claim 30, wherein the substance is selected from the group consisting of:

a) antibodies directed against VGF proteins, VGFARP peptides, NGF, BNDF or NT-3;

b) antisense nucleic acids, triplex nucleic acids or ribozymes that reduce expression of VGF proteins, VGFARP peptides, NGF, BNDF or NT-3;

c) substances that inhibit processing of VGF proteins; and

d) antagonists of VGFARP peptides or VGF proteins.

35. (Original) The method of claim 30, wherein the substance is selected from the group consisting of:

a) VGF proteins, VGFARP peptides, NGF, BNDF or NT-3;

b) nucleic acids which code for VGF proteins, VGFARP peptides, NGF, BNDF or NT-3;

c) substances which promote the processing of VGF proteins, and

d) agonists of the VGFARP peptides or of VGF proteins.

36. (Original) The method of claim 30, wherein the substance modulates the expression of at least one VGF protein.

37. (Original) The method of claim 36 wherein the VGF protein is selected from the group consisting of NGF, BNDF and NT-3.

38. (Original) The method of claim 30, wherein the substance selectively inhibits or stimulates the transcription or expression of at least one VGF protein.

39. (Original) The method of claim 30, wherein the substance binds to at least one VGF protein or VGFARP peptide.

40. (Original) The method of claim 39 wherein the substance is selected from the group consisting of antibodies, antibody fragments, and affinity matrices.

41. (Original) The method of claim 30 wherein the substance is administered via an administration route selected from the group consisting of: the bloodstream, the gastrointestinal tract, the urogenital tract, the lymphatic system, the subarachnoid space, the lungs, and direct injection into tissue.

42. (Original) The method of claim 41, wherein the tissue is selected from the group consisting of muscle tissue, adipose tissue, and brain tissue.

43. (Original) The method of claim 30, wherein the substance has been pharmaceutically processed or chemically or biologically modified to cross the blood-brain barrier and/or the blood-CSF barrier.

44. (Original) A VGFARP peptide.

45. (Original) The VGFARP peptide of claim 44, wherein the VGFARP peptide is a derivative of a VGF protein.

46. (Original) The VGFARP peptide of claim 45, wherein the VGFARP peptide is a derivative of a VGF allele.

47. (Original) The VGFARP peptide of claim 44, wherein the VGFARP peptide is a mutant VGFARP peptide that differs by a maximum of 2 amino acids from the corresponding unmutated VGFARP peptide.

48. (Original) The VGFARP peptide of claim 44, wherein the sequence of the VGFARP peptide is selected from the group consisting of: SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:41, and SEQ ID NO:42.

49. (Original) The VGFARP peptide of claim 45, wherein said VGFARP peptide is a derivative of a VGF protein represented by SEQ ID NO:43 or SEQ ID NO:44.

50. (Original) The VGFARP peptide of claim 44, wherein said peptide is chemically or post-translationally modified.

51. (Original) A nucleic acid molecule that encodes a VGFARP peptide.

52. (Original) A nucleic acid molecule that is the complement of a nucleic acid molecule that encodes a VGFARP peptide.

53.(Original) A pharmaceutical composition comprising,

at least one VGF protein or VGFARP peptide, a nucleic acid encoding at least one VGF protein or VGFARP peptide, or a nucleic acid that is the complement of a nucleic acid encoding at least one VGF protein or VGFARP peptide.

54. (Original) A diagnostic reagent for the detection of neurological diseases, comprising, antibodies to at least one VGF protein or VGFARP peptide, and

a suitable carrier.

55. (Original) The diagnostic reagent of claim 54, wherein the neurological disease is selected from the group consisting of a neurological disease, chronic dementia, and Alzheimer's disease.

56. (Original) Antibodies that bind to VGFARP peptides.

57. (Original) Nucleic acids that are VGF-specific antisense nucleic acids, components of VGF-specific ribozymes, or VGF-specific triplex nucleic acids.